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PATENT/Docket No.: 4121.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

121-11-21-86

Art Unit	:	121
Examiner	:	
Applicant(s)	:	M.I. Amin et al.
Serial Number	:	898,676
Filed	:	21 August 1986
For	:	CRYSTALLINE CEPHALOSPORIN HYDROHALIDE HEMIALCOHOLATE

Commissioner of Patents and Trademarks
Washington, DC 20231

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR 1.97 AND 1.98

Sir:

Provided herewith are copies of patents and publications as listed in the attached form PLD-1449. A concise explanation of the relevance of each reference listed in form PLD-1449 is:

[X] contained in the above-captioned specification as filed; and/or

[X] provided in a communication enclosed with this paper.

Applicant respectfully asserts that the substantive provisions of 37 CFR 1.97 and 37 CFR 1.98 are met by the provision of the foregoing statement.

Respectfully submitted,

10 December 1986
Date

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Attachment: PLD-1449

PLD-97.1
9/86

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Art Unit	:	121
Examiner	:	
Applicant(s)	:	M.I. Amin et al.
Serial Number	:	898,676
Filed	:	21 August 1986
For	:	CRYSTALLINE CEPHALOSPORIN HYDROHALIDE SALTS

Commissioner of Patents and Trademarks
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COMMUNICATION

Sir:

Provided herewith are copies of patents and publications as listed in the attached form PLD-1449. An explanation of the relevance of the references, as numbered on the form PLD-1449, is as follows:

1-25, 31-33. The U.S. Patent Documents numbered 1-25 and the Foreign Patent Documents numbered 31-33, disclosing various cephalosporin compounds having an amino group in the 7-position side chain thereof, have been quickly reviewed for any possible pertinence to the hydrohalide product and process claims in this application. The closest patents in this collection are believed to be U.S. Patent Documents numbered 9, 20 and 22.

9. The Takaya et al. 4,254,260 patent (1) discloses cephalosporins with protected amino groups on heterocyclic rings in the 7-side chain acyl groups, (2) refers to numerous protecting groups in column 8 and the removal thereof by various chemical means in column 16, but this '260 patent does not teach Applicants' compound or how to obtain the crystalline of Applicants' compound.

20. The Heymes et al. 4,297,352 patent discloses the removal of a trityl protecting group and an ester group with trifluoroacetic acid in Example 1 thereof, but it does not teach how to obtain the hydrohalide salt product of this invention or the process of this invention.

22. The Natsugari et al. 4,298,607 patent discloses a crystalline hemi-acid, hydrochloride or hydrobromide salt of a compound, now referred to in the 1984 "USAN and the USP Dictionary of Drug Names" (copy provided below) as "cefmenoxime hydrochloride." This '607 patent discloses the treatment of the

sodium salt of the cephalosporin with hydrochloric acid at 23°-25°C. The crystals are obtained and dried at room temperature to 25°C. There is no reference to the need for higher temperatures. No trityl group removal step is referred to. Hence, this '607 patent tells one nothing about how to obtain the crystalline form of the hydrohalide salt of ceftiofur of this invention.

26. The Labeeuw et al. 4,464,367 patent is discussed in the specification as filed at page 1, lines 9-17.

27. The Yang U.S. Patent 4,400,503 discloses a crystalline hydrochloride salt of another cephalosporin antibiotic, but it does not disclose Applicants' compound or predict in any way how to make the crystalline salt of Applicants' compound.

28. The Bryan U.S. Patent 4,034,099 discloses pharmaceutical vehicles with which the compound of this invention can be mixed for antibiotic use purposes. It is also discussed in the specification as filed at page 6, lines 7-9.

29. The Scartazzini U.S. Patent 4,411,897 discloses a crystalline hydrobromide salt of a specific 3-hydrogen-cephalosporin pivaloyloxymethyl (tert-butoxymethyl)ester. Applicants' compounds are not esters.

30. The Derwent Abstract of U.S. Patent 4,594,417A discloses the same crystalline cephalosporin hydrochloride salt as disclosed in Yang et al above.

34. The Derwent Abstract of German Patent 3037-104-C discloses the stable crystalline bis-hydrochloride of coftazidime.

35. The Derwent Abstract of J8 6013-479-B discloses a process for crystallizing prismatic crystals of cefalexin hydrate.

36. The Derwent Abstract of EP 33-518 discloses crystalline 7β-[2-(2-amino-4-thiazolyl)-2-methoxyimino-acetamido]-3-cephem-4-carboxylic acid pivaloyloxy methyl ester hydrochloride and hydrobromide salts.

37. The trade publication is discussed in the specification as filed at page 6, lines 9-15.

38. The Curran article in the Journal of Antibiotics is discussed in the specification as filed at page 6, lines 29-31.

39. The Tetzlaff et al., Journal of Pediatrics article was attached to the Invention Report, and relates to the cephalosporin antibiotic cephalexin, but is not believed to be pertinent to Applicants' invention.

40. The C.M. Ginsburg et al., Journal of Pediatrics article was attached to the Invention Report. It relates to two cephalosporin antibiotics, cefaclor and cefadroxil, but is not otherwise believed to be pertinent here.

41. The R. Oberholtzer et al., Journal of Pharmaceutical Sciences article was attached to the Invention Report. It refers to a cephalosporin antibiotic, cefoxitin sodium salt, but is not believed to be otherwise pertinent hereto.

42. The M.J. Pikal et al., Journal of Pharmaceutical Sciences article reports on the thermal decomposition of salts of several β-lactam antibacterial compounds, including some penicillin and cephalosporin salts, in their amorphous and unsolvated crystalline forms as a function of temperature and water content. This publication was attached to the Invention Report here, but it does not disclose Applicants' compound here, or anything about the properties of Applicants' compound here.

43. The W. Durckheimer et al., article discloses a highly active sulphoxide of the cephalosporin cefotaxime, but is not believed to be pertinent to this invention.

44. The Abstract of the Vignau article discloses the preparation of a particular 7-[2-(2-aminothiazol-4-yl)acetamido]-3-carbamoyloxymethyl-3-cephem-4-carboxylic acid prepared by acylating 7-aminocephalosporanic acid with a mixed anhydride of 2-(trityl-protected-aminothiazol-4-yl)acetic acid and isopropyloxychloroformate in a methanol/sodium methoxide mixture followed by removal of the trityl group by heating the protected compound with aqueous acetic acid. This reference does not refer to a hydrohalide salt.

45. The T.W. Greene textbook teaches generally about the removal of a trityl group from an amine with hydrogen chloride at room temperature (25°C).

46. The T. Yamana et al., article describes the relative stability of six commercial cephalosporins in acid solutions.

47. The pages from the USAN and the USP Dictionary of Drug Names shows the cefmenoxime hydrochloride compound of the Natsugari et al patent above.

Respectfully submitted,

Date: 10 Dec. 1986

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